IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Johannes BARTHOLOMÄUS et al.
Application No.: 10/718,112
Filed: November 20, 2003
For: ABUSE-PROOFED DOSAGE FORM

DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Dr. Johannes Bartholomäus, hereby declare in lieu of an oath the following:

1. I am a citizen of Germany, residing at Burghöhenweg 5, D-52080 Aachen, Germany.

2. I am a pharmacist and received a PhD degree in pharmacy.

3. I have been employed by Grünenthal GmbH since August 1, 1988, since 1992 as head of the department for pharmaceutical development.

4. I am one of the inventors of the invention disclosed in the U.S. Patent Application Serial No. 10/718,112. The abuse-proofed, thermoformed dosage form described in U.S. Patent Application Serial No. 10/718,112 has been developed under my supervision and control.

5. A breaking strength of 500 N is far above the typical breaking strength of conventional pharmaceutical dosage forms. Conventional dosage forms typically have breaking strengths well below 200 N.

6. The mean chewing force is well below 500 N but high enough so that conventional pharmaceutical dosage forms can be crushed by chewing. Dosage forms having a breaking strength of at least 500 N, however, cannot be crushed by chewing.

7. I have read *Alaux et al.* (WO 00/33835), *Kuczynski et al.* (US 5,866,164), *Oshlack et al.* (US 2003/0064099), *Porter* (US 4,175,119), *Miller et al.* (US 5,849,240) and *Sackler* (US 2004/0170567) which were cited in examination proceedings of U.S. Patent Application Serial No. 10/718,112. I cannot find any hint in these references, neither explicit nor implicit, which might lead a skilled artisan to thermoformed pharmaceutical dosage forms containing polyalkylene oxide having a molecular weight of at least 0.5 million and having a breaking strength of at least 500 N.

8. The following experiments were conducted under my supervision and control:

Round tablets having a diameter of 10 mm, a radius of curvature of 8 mm and a mass of 333.0 mg were prepared from mixtures of the following components:

components	# 1		# 2	
	[mg]	[wt.-%]	[mg]	[wt.-]
Tramadol HCl	83.25	25.0	83.25	25.0
polyethylene oxide (M_w 0.6 million)	249.75	75.0	-	-
polyethylene oxide (M_w 7 million)	-	-	249.75	75.0

Tramadol HCl and polyethylene oxide were weighed and mixed for 15 minutes in a rolling glass mixer at 14 Rpm. Then, the mixtures were compressed on a Korsch EK0 (punch format 10 mm, radius of curvature 8 mm) at two different pressure forces. The breaking strength was measured by means of a Zwick breaking strength tester (average value over 10 tablets).

The results of the measurements are summarized in the table here below:

	# 1 M_w 0.6 million		# 2 M_w 7 million	
pressure force	≈ 7000 N	≈ 40000	≈ 5000	≈ 38000
breaking strength	**94.2 N**	**145.1 N**	**54.0 N**	**121.1 N**

As demonstrated by the above tests, direct compression of pharmaceutical compositions that contain polyalkylene oxide having a molecular weight of at least 0.5 million on a conventional tablet press under conventional conditions does not yield dosage forms having a breaking strength of at least 500 N.

9. All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true, and further, these statements were made with the knowledge that willful false statements and the like, so made, are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the U.S. Patent Application Serial No. 10/718,112 or any patent issued thereon.

May 3rd, 2007 — (Date)

(Dr. Bartholomäus, Johannes)